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## Murine Tissue-Engineered Stomach Demonstrates Epithelial Differentiation.

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### Public Summary:

Tissue-engineered stomach is a potential replacement solution to restore adequate food reservoir and gastric physiology. In this study, we performed a detailed investigation of the development of tissue-engineered stomach in a mouse model, specifically evaluating epithelial differentiation, proliferation, and the presence of putative stem cell markers. This study demonstrates the successful generation of tissue-engineered stomach in a mouse model for the first time. Regenerated gastric epithelium is able to appropriately proliferate and differentiate. The generation of murine tissue-engineered stomach is a necessary advance as it provides the transgenic tools required to investigate the molecular and cellular mechanisms of this regenerative process. Delineating the mechanism of how tissue-engineered stomach develops in vivo is an important precursor to its use as a human stomach replacement therapy.

### Scientific Abstract:

**BACKGROUND:** Gastric cancer remains the second largest cause of cancer-related mortality worldwide. Postgastrectomy morbidity is considerable and quality of life is poor. Tissue-engineered stomach is a potential replacement solution to restore adequate food reservoir and gastric physiology. In this study, we performed a detailed investigation of the development of tissue-engineered stomach in a mouse model, specifically evaluating epithelial differentiation, proliferation, and the presence of putative stem cell markers. **MATERIALS AND METHODS:** Organoid units were isolated from <3 wk-old mouse glandular stomach and seeded onto biodegradable scaffolds. The constructs were implanted into the omentum of adult mice. Implants were harvested at designated time points and analyzed with histology and immunohistochemistry. **RESULTS:** Tissue-engineered stomach grows as an expanding sphere with a simple columnar epithelium organized into gastric glands and an adjacent muscularis. The regenerated gastric epithelium demonstrates differentiation of all four cell types: mucous, enteroendocrine, chief, and parietal cells. Tissue-engineered stomach epithelium proliferates at a rate comparable to native glandular stomach and expresses two putative stem cell markers: DCAMKL-1 and Lgr5. **CONCLUSIONS:** This study demonstrates the successful generation of tissue-engineered stomach in a mouse model for the first time. Regenerated gastric epithelium is able to appropriately proliferate and differentiate. The generation of murine tissue-engineered stomach is a necessary advance as it provides the transgenic tools required to investigate the molecular and cellular mechanisms of this regenerative process. Delineating the mechanism of how tissue-engineered stomach develops in vivo is an important precursor to its use as a human stomach replacement therapy.

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